Remarks:

The 04/13/2007 Office action provided the following items:

Restriction Requirement: Applicant was requested to elect between Group I covering compounds (products) and Group II covering methods of using the products, with the clarification that method claims commensurate in scope with the elected products will be rejoined at such time that the claims drawn to the elected products are in condition for allowance. From the course of the application, the product claims (claims 36 to 47) were constructively elected and claims 48 to 51 were withdrawn from consideration.

Rejection based on 35 USC 112, first paragraph: The inclusion of "solvates of" was rejected for claims 36 to 47. It was clarified that if this phrase were removed, the compound claims would be allowed. In making this rejection, the Examiner looked to the *Wands* factors from *In re Wands*, 858 F.2d 731, 737; 8 USPQ2d 1400, 1404 (Fed. Cir. 1988):

Regarding the breadth of claims, the Examiner cited the definition of a solvate taken from the Vippagunta et al reference alleging a solvate is a "crystalline solid adduct[s] containing solvent molecules within the crystal structure, in either stoichiometric or nonstoichiometric proportions, giving rise to unique differences in the physical and pharmaceutical properties of the drug." It was alleged that the claims would read on a huge number of special solid forms of the compounds, because there are so many different solvents known to those of ordinary skill in the chemical arts.

Regarding the nature of the invention, it was alleged that the nature of the invention is that of a chemical compound, a pharmaceutical composition or a medical treatment method, wherein the compound is in a special physical form.

Regarding the state of the art, the level of ordinary skill and the level of predictability in the art, it was alleged that solvates, at the time the invention was made, were known to exist and could be identified, and many had indeed been documented in the literature, but the level of skill in the art had not progressed to such an extent that the directed preparation of those solvates other than hydrates was routine or simple. It was also alleged that formation of specific crystalline forms, and more particularly solvates, was highly unpredictable.

It was alleged that no guidance relevant to preparation of solvates is provided in the disclosure, and that no working examples demonstrated the preparation of a solvate.

Regarding the amount of experimentation needed to make or use the invention based on the content of the disclosure, it was alleged that "[f]or one of ordinary skill in the art to conduct the type of research outlined in Gavezzotti and in Vippagunta et al for preparation of every one of the claimed solvates would be undue. 'A solvate' of a chemical compound is much more complex than simply a mixture of a compound with some solvent. A grant to applicants of a right to exclude others from making all solvates of compounds embraced by the instant claims is unwarranted in light of the complete lack of any direction as to how one of ordinary skill would do so."

Method claims: If the compound claims were allowed, the method claims could be rejoined except it was alleged that some of the diseases listed had nothing to do with dopamine or serotonin receptors of any kind. It was recommended to cancel claims 48 and 50 and to amend claims 49 and 51 so as to limit those claims to a method of treating a disorder selected from the group consisting of schizophrenia, a schizophreniform disorder, a schizoaffective disorder, a delusional disorder, a substance-induced psychotic disorder, a personality disorder of the schizoid type, dementias, a schizoaffective disorder of the delusional type or the depressive type, psychosis induced by alcohol, amphetamine, cannabis, cocaine, hallucinogens, inhalants or phencyclidine (opioids do not cause psychosis, and therefore "opioids" should be struck from this part of the Markush group), multi-infarct dementia, dementia associated with intracranial tumors or cerebral trauma, dementia associated with Huntington's disease or Parkinson's disease, or AIDS-related dementia, Alzheimer's-related dementia, delirium and Tourette's syndrome.

Arguments:

Restriction Requirement: Applicant accepts the constructive election of Group I with traverse. It is Applicant's position that searching both groups would not be unduly burdensome.

Rejection based on 35 USC 112, first paragraph:

Applicant respectfully traverses this rejection. It is Applicant's position that the definition alleged in the pending office action for solvate is too narrow and is inconsistent with the ordinary and customary meanings.

The enablement rejection evolves around the scope of the claims. When defining "solvate" in the pending office action, reference is made to a "crystalline" form, citing Vippagunta, et al. The discussion of Vippagunta concerns identifying the most stable form of a compound for development. The focus of the research discussed by Vippagunta et al. is for understanding the solid-state area to predict the most stable drug form for development. The definition being proposed in the pending office action misconstrues the invention. The MPEP states: "During patent examination, the pending claims must be given the broadest reasonable interpretation consistent with the specification. *In re Morris*, 127 F.3d 1048, 1054, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997); *In re Prater*, 415 F.2d 1393, 162 USPQ 541 (CCPA 1969). See also MPEP § 2111 - § 2111.01." MPEP 2173.05(a), I.

The MPEP states: "In the absence of an express intent to impart a novel meaning to the claim terms, the words are presumed to take on the ordinary and customary meanings attributed to them by those of ordinary skill in the art." MPEP 2111.01, III, citing *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1298 67 USPQ2d 1132, 1136 (Fed. Cir. 2003).

> It is the use of the words in the context of the written description and customarily by those skilled in the relevant art that accurately reflects both the "ordinary" and the "customary" meaning of the terms in the claims. *Ferguson Beauregard/Logic Controls v. Mega Systems*, 350 F.3d 1327, 1338, 69 USPQ2d 1001, 1009 (Fed. Cir. 2003) (Dictionary definitions were used to determine the ordinary and customary meaning of the words . . . to those skilled in the art. In construing claim terms, the general meanings gleaned from reference sources, such as dictionaries, must always be compared against the use of the terms in context, and the intrinsic record must always be consulted to identify which of the different possible dictionary meanings is most consistent with the use of the words by the inventor.) . . . . [MPEP 2111.01, III].

The present invention concerns compounds made and identified to be useful to treat the indications provided in the pending application. Therefore, Applicant directs attention to Dorland's Illustrated Medical Dictionary where "solvate" is defined as "[a] compound of one or more molecules of a solvent with the ions or with the molecules of a dissolved substance." Dorland's Illustrated Medical Dictionary, 1404, 24th Ed. 1965 (attached hereto). This is

consistent with the general definition in the Merriam-Webster Dictionary that defines "solvate" as "an aggregate that consists of a solute ion or molecule with one or more solvent molecules; also: a substance (as a hydrate) containing such ions". Merriam-Webster Dictionary Online, August 7, 2007 (http://www.m-w.com/dictionary/solvate). These general definitions are appropriate for the pending application. Therefore, the remaining analysis will be done with these general definitions as they relate to Applicant's invention encompassing compounds of formula I, the salts thereof and solvates of said compounds or salts thereof. Thus, the science involved with the pending invention concerns making and isolating several compounds for structure-activity-relationship studies (SARs).

It was alleged that the claims read on a huge number of special solid forms of the compounds, because there are so many different solvents known to those of ordinary skill in the chemical arts. However, one of ordinary skill in the chemical arts concerned with SARs would appreciate possible solvents acceptable for isolation of the compounds and salts thereof prepared in the pending application.

The state of the prior art should concern how the term solvate is used with regard to compounds involved with SARs. The pending office action has incorrectly focused on crystalline forms of specific compounds for advanced drug development, further citing Gavezzotti regarding the prediction of polymorphs. Applicant's invention has not been appreciated. An organic chemist in the field of making, isolating and identifying compounds for SARs would use standard chemistry procedures to make and isolate many compounds. This process involves removing solvent by standard chemistry procedures, e.g., by evaporation under vacuum, to obtain the title compounds for structure confirmation. Residual solvent is commonly present when isolating such compounds. The technique has been around for many years. It is not only predictable, but it is expected that compounds isolated as described in the specification will have residual solvent. Furthermore, it is common practice, when providing spectral data of isolated compounds, not to provide peaks for residual solvent but to provide those peaks associated with compound identification for confirmation that the title compound was actually made.

Regarding the amount of direction and number of working examples required in the pending application, the MPEP states:

> The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'." *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). [MPEP 2164.08.]

The MPEP states elsewhere: "The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation." *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970). MPEP 2164.02.

Because the solvate aspect of the invention is standard procedure within organic chemistry, especially as it relates to making compounds for SARs, it is Applicant's position that the experimentals discussing the isolation of the compounds provides the examples and direction required to satisfy 35 USC 112, first paragraph. Furthermore, because of the standard procedures to obtain the solvates of the compounds of formula I and salts thereof, there is no undue experimentation involved to achieve the claimed invention as it relates to solvates of the compounds of formula I and salts thereof.

Applicant respectfully requests withdrawal of the rejection based on 35 USC 112, first paragraph.

Method Claims:

Applicant is not able to locate one of the references cited in the pending office action: Hirota et al, "Neuropharmacololgical Profile of an Atypical Antipsychotic, NRA0562" CNS Drug Reviews, vol. 9(4), pages 375-388 (2003). Regardless of this, to advance prosecution, Applicant has canceled claims 48 and 50 and has amended the claims 49 and 51 to cover the diseases cited in the pending office action as being allowable. In so doing, Applicant makes no admission of the lack of support for the canceled subject matter, and Applicant reserves the right to file any subsequent application on canceled/deleted subject matter and present any arguments available. Applicant believes that the amended claims obviate the pending rejection. Applicant respectfully requests withdrawal of said rejection for claims 48 to 51.

Applicant requests a copy of said reference for future purposes.

Conclusion

Applicant believes that the claims are in order for allowance, early notice of which is requested. If Examiner has any questions concerning this application, Examiner is invited to contact the below-signed attorney. A fee is due; please charge any payment or credit any overpayment to Charge Account 16-1445.

Respectfully submitted,

___/Mary J. Hosley/_____ Date: _____13 August 2007___
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DORLAND'S ILLUSTRATED

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normal s., a solution each liter of which contains 1 gram equivalent weight of the active substance: designated N/1 or 1 N. **normal saline s., normal salt s.**, physiological salt s. **normobaric s.**, isobaric s. **Orth's s.**, a solution for fixing histological specimens, consisting of Müller's fluid and formaldehyde solution. **parathyroid s.**, parathyroid injection. **Pasteur's s.**, a solution of ammonium tartrate, cane sugar, and ash from yeast, in water: used as a medium for growing yeasts and molds. **Perenyi's s.**, an embryological fixing solution, consisting of 10 per cent solution of nitric acid, alcohol, and 0.5 per cent solution of chromic acid. **phenylephrine hydrochloride s.**, a clear, colorless, or slightly yellow liquid, which contains 95-105 per cent of the labeled amount of phenylephrine hydrochloride. **physiological salt s., physiological sodium chloride s.**, an aqueous solution of sodium chloride and other components, having an isosmotic pressure identical to that of blood serum. **Pickrell's s.**, a solution of sulfadiazine in ethanolamine, with sodium benzoate as preservative. **Pitkin's s.**, a solution of procaine in a solvent having a specific gravity lower than that of the spinal fluid: used as a spinal anesthetic. **pituitary s., pituitary posterior**, posterior pituitary injection. **potassium arsenite s.**, a solution of arsenic trioxide, potassium bicarbonate, and alcohol in water, used as an antileukemic agent. **potassium iodide s.**, a clear, colorless, odorless liquid with a strongly salty taste and neutral or alkaline reaction, each 100 ml. of which contains 97-105 Gm. of potassium iodide. **racephedrine hydrochloride s.**, a clear, colorless solution with a camphoraceous odor and taste, compounded of racephedrine hydrochloride, chlorobutanol, and Ringer's solution. **radiocyanocobalamine s.**, a solution suitable for oral administration, containing cyanocobalamin labeled with cobalt-60: used as an aid in diagnosing pernicious anemia. **radiogold s.**, a colloidal solution of radioactive gold (Au^{198}): used as a neoplastic suppressant. **Rees-Ecker s.**, a solution consisting of sodium citrate, neutral formaldehyde, and brilliant cresyl blue: used as a diluting fluid for direct platelet counts. **Ringer's s.**, a clear, colorless liquid, with a mild saline taste, containing, in each 100 ml., 820-900 mg. of sodium chloride, 25-35 mg. of potassium chloride, and 30-36 mg. of calcium chloride, prepared with recently boiled purified water: for topical use. **Ruge's s.**, a solution of glacial acetic acid, 40 per cent formalin, and water: used as a stain. **saline s., salt s.**, a solution of sodium chloride, or commonly, 0.9 per cent in water. **saponated cresol s.** See *cresol s., saponated.* **saturated s.**, a solution in which the solvent has taken up all of the dissolved substance that it can hold in solution. **Schaffenburn's s.**, a solution of colloidin and oil of cloves: used in histological work to attach paraffin sections to slides. **sclerosing s.**, a solution of an irritant substance for injection into a vein to produce obliteration of the vein, or into a tissue to induce fibrous formation and obliteration of the sac. **seminormal s.**, half normal s. **Seyderheim's s.**, a colloidal mixture of Congo red and trypan blue, for staining urinary sediment. **silver nitrate s., ammoniacal**, a clear, colorless, almost odorless liquid, compounded of silver nitrate, water, and strong ammonia solution: used as a dental protective. **silver nitrate ophthalmic s.**, a solution of silver nitrate in a buffered water medium, containing 0.95-1.05 per cent of $AgNO_3$: used as a local antiinfective applied topically to the conjunctiva. **sodium borate s., compound**, a solution containing sodium borate, sodium bicarbonate, liquefied phenol, glycerin, and purified water: used as a gargle or mouth wash. **sodium chloride s.**, a sterile solution of sodium chloride in purified water, containing 0.85-0.95 per cent of NaCl: topical use only. **sodium citrate anticoagulant s.**, a sterile solution of sodium citrate in water: used to prevent coagulation of blood plasma and of whole blood. **sodium hypochlorite s.**, a clear, pale, greenish yellow liquid with the odor of chlorine, containing 4-6 per cent of sodium hypochlorite. **sodium hypochlorite s., diluted**, a colorless to light yellow liquid with a faint odor of chlorine, compounded of sodium hypochlorite solution, sodium bicarbonate, and water, each 100 ml. containing 450-500 mg. of NaClO. **sodium phosphate s.**, a clear colorless liquid without odor and with a salty taste, the consistency of thick syrup, each 100 ml. of which contains the equivalent of 71-79 Gm. of sodium hyposphate. **sodium radio-iodide s.**, a solution containing radioactive iodine (I^{131}), used in diagnostic studies of thyroid disease and in detection and treatment of thyroid carcinoma. **sodium radio-phosphate s.**, a solution containing radioactive phosphorus (P^{32}): used as a suppressant of certain neoplasms and polycythemia. **sorbitol s.**, a clear, colorless, syrupy liquid with a sweet taste and without odor, recommended as a sweetening agent for diabetics and as a diuretic, and used in various pharmaceutical preparations. **standard s.**, one which contains in each liter a definitely stated amount of reagent; usually expressed in terms of normality (equivalent weight of active substance per liter of solution). **sufurated lime s.** See *lime s., sulfurated.* **supersaturated s.**, a solution that contains in solution more of the solute than it can permanently hold. **surgical s. of chlorinated soda.** See *sodium hypochlorite s., diluted.* **susa s.**, a decalcifying solution composed of corrosive sublimate, sodium chloride, trichloracetic acid, glacial acetic acid, formalin, and water. **tenth-normal s.**, one having one-tenth the strength of a normal solution: designated N/10 or 0.1 N. **test s's**, standard solutions of specified chemical substances used in performing certain test procedures. **thousandth-normal s.**, a solution having one-thousandth the strength of a normal solution: designated N/1,000 or 0.001 N. **Toison's s.**, a fluid used in diluting blood for the counting of the erythrocytes, consisting of crystal violet, sodium chloride, sodium sulfate, glycerin, and water. **tribromoethanol s.**, a clear colorless liquid, a solution of tribromoethanol in amylene hydrate, each 100 ml. of which contains 99-101 Gm. of tribromoethanol. **tribromoethyl alcohol s.**, tribromoethanol s. **Tyrode's s.**, a modified Locke's solution containing magnesium, used especially for perfusing the intestine of the rabbit. **tyrothricin s.**, a solution of tyrothricin in alcohol. **Uschinsky's s.**, a solution in water of asparagin, ammonium lactate, neutral sodium phosphate, and sodium chloride: used as a culture medium for bacteria. **Vieminckx' s.**, lime s., sulfurated. **volumetric s.**, one which contains a specific quantity of solvent per stated unit of volume. See also *standard s.* **Winogradsky's s.** 1. *For growing nitrifying organisms:* Potassium phosphate, magnesium sulfate, calcium chloride, sodium chloride, and ammonium sulfate, in water. 2. *For growing nitrosifying organisms:* Ammonium sulfate, potassium sulfate, and basic magnesium carbonate, in water. **Zenker's s.**, a fixative solution consisting of mercury bichloride, potassium dichromate, glacial acetic acid, and water. **Ziehl's s.** See *Table of Stains and Staining Methods.*

solv. Abbreviation for L. *solve*, dissolve.

solvable (sol'vah-b'l). Soluble.

solvate (sol'vāt). A compound of one or more molecules of a solvent with the ions or with the molecules of a dissolved substance.

solvation (sol-va'shun). Chemical combination of a solvent with the solute.

solvent (sol'vent) [L. *solvens*]. 1. Dissolving; effecting a solution. 2. A liquid that dissolves or that is capable of dissolving.

solvolysis (sol-vol'i-sis). A general term for double decomposition reactions of the type of hydrolysis, ammonolysis, and sulfolysis.

soma (so'mah) [Gr. *sōm* tinguished from the m distinguished from the for preparations of ca

somacule (so'mah-kūl ticle of protoplasm.

somal (so'mal). Pertair

somaplasm (so'mah-p

somasthenia (sōm"as + Gr. *sthenos* streng bodily weakness, poor ability to maintain a easy exhaustion.

somatalgia (so"mah- *algos* pain + *-ia*]. Bodi

somatasthenia (so". thenia.

somatesthesia (so"m Gr. *aisthesis* perceptio of having a body.

somatesthetic (so"ma somatesthesia.

somatic (so-mat'ik) [G or characteristic of the

somatopsychonic Somaticovisceral.

somaticovisceral (s taining to the body an

somatist (so'mah-tist that neuroses and psy and are based on bodil

somatization (so"mah the conversion of ment bodily symptoms.

somato- (so'mah-to) Combining form den body.

somatoceptor (so-ma concerned in receiving somatic musculature.

somatochrome (so-ma *chroma* color]. Any n marked cell body com cleus, its colorable pe contour; used also adj

somatoderm (so-mat *derma* skin]. The soma

somatodidymus (so"t monster exhibiting son

somatodymia (so"ma Gr. *didymos* twin + -*ia* aly resulting in the pro whose trunks are fused

somatogenesis (so"m Gr. *genesis* production genee of bodily structur the formation of somat

somatogenetic (so-ma ing to somatogenesis.

somatogenic (so"mah *gennan* to produce]. Or body.

somatogram (so-mat *gramma* a writing]. A r

somatology (so"mah-t The sum of what is k the study of the anato body.

somatome (so'mah-tōm cut]. 1. An appliance f fetus. 2. A somite.

somatomegaly (so"m + Gr. *megaleos* stately body; gigantism.

somatometry (so-mah *metron* measure]. Measu

somatomic (so"mah-t somatome.

somatopagus (so"mal